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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/797,019

03/11/2004

Bradley A. Saville

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20736 7590 10/18/2007

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EXAMINER

GOUGH, TIFFANY MAUREEN

ART UNIT

PAPER NUMBER

1657

MAIL DATE

DELIVERY MODE

10/18/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/797,019

Applicant(s)

SAVILLE ET AL.

Examiner

Tiffany M. Gough

Art Unit

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 9-16 and 19-42 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-16 and 19-42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 5/2/2007.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/2/2007 has been entered.

Claims 1-7,9-16,19,20 and new claims 21-42 are pending and have been considered on the merits. All arguments and amendments have been considered.

### ***Information Disclosure Statement***

The information disclosure statement filed 3/11/2004 fails to comply with 37 CFR 1.98(a)(2), which **requires a legible copy of each cited foreign patent document;** each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Applicant argues in the replied filed 5/2/2007 that the IDS complies and full consideration is requested. Applicant has not provided the office with copies of **each cited foreign patent document.**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7,9-16,19-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite a method of enhancing enzymatic activity of an enzyme. Thus, the claims encompass the enzymatic enhancement of numerous potential enzymes, for which no written description has been provided. Moreover, the sole examples using alpha amylase and glucoamylase does not provide a representative sample of the enzymes encompassed by the claims, given the huge variation in characteristics, structural, and chemical properties encompassed by the current broad claim language. Because the claims encompass a multitude of enzymes neither contemplated nor disclosed by the as-filed disclosure, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

Claims 21, 31,42 and their dependent claims 22-30,32-41 and its dependents are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the amendment of claims 21,31 and 42 to read, "...if the enzyme solution contains cells, filtering the diluted enzyme solution to remove the cells;"

introduces new matter, which is not described in the specification as originally filed.

Claim 24,34 requires that "the diluted enzyme exhibit at least the same level of enzyme activity per equal volume of the ...", this introduces new matter. Claim 25,35 states that the solution is enhanced by at least 200%, this also introduces new matter. Claims 29,41 requires that the pH of the solution maintains enzyme activity, this additionally introduces new matter.

Applicant states on p.1 of the argument submitted 5/2/2007 that the basis for claims 24,25,34 and 35 can be found by combining the teachings on page 4, lines 15-16 of the specification, however, there is no such support for the claims on p.4. Applicant also fails to provide direction to support in the specification for the other new claims and limitations. **This is a new matter rejection.**

Claims 1-7,9-16,19-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enhancement of enzymatic activity of the enzyme amylase, i.e. alpha and glucoamylase, does not reasonably provide enablement for enhancing the enzymatic activity of **any and all** enzymes by the claimed method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Specifically, as discussed above with respect to the issue of written description, the claims recite a method of enhancing enzymatic activity of an enzyme. The claims therefore encompass the enzymatic enhancement of numerous potential enzymes, for which no written description has been provided. Moreover, the sole examples using alpha amylase and glucoamylase does

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not provide a representative sample of the enzymes encompassed by the claims, given the huge variation in characteristics, structural, and chemical properties encompassed by the current broad claim. Given the property differences among enzymes such as structure, function and, one of ordinary skill in the art would not expect to be able to apply the disclosed method to any and all enzymes encompassed by the current claim language. Further, **applicants own arguments support** such lack of enablement.

Page 12 of the arguments submitted 5/2/2007 states "because of structural and functional differences between proteins, an ideal sequence of steps for one protein will, quite possibly, be unsuccessful for another..." applicant also states on p.12, that "it is apparent that the procedure is not automatic-the fact that a procedure works provides no guarantee that it will work for another enzyme." Thus, with the exception of the above stated enzymes, and in view of the lack of any specific guidance with respect to the reaction conditions other than what is encompassed by the claims, one skilled in the art would expect a trial and error process to determine which enzymes encompassed by the claims would apply to the as disclosed application, and would further have to determine through undue experimentation, without guidance from the specification, how to perform such a method using any and all enzymes.

Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary to test each and every enzyme encompassed by the claim language, limited amount of guidance and limited number of working examples in the specification using a variety of enzymes; nature of the

invention; state of the prior art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7,9-16 **stand** rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Particularly claim 1 and its dependent claims are confusing and fails to distinctly claim applicants invention because, it reads, “ a method of enhancing the... activity of an enzyme to a substrate susceptible to said enzyme...” It appears as if steps or words have been eliminated from the method as claimed.

Applicant argues that claim 1 was amended to provide antecedent basis for the word “substrate” in claim 20. Claim 20 does not depend on claim 1, therefore applicant's arguments do not provide any clarification of the previous rejection. The rejection was made based on the language of claim 1, i.e. “A method of enhancing the intrinsic activity of an enzyme to a substrate susceptible to said enzyme...” The sentence is incomplete, i.e. there must be words missing between “enzyme” and “to” for one to make any sense of such sentence. **Applicant's arguments are not persuasive and the claim does not fully comply with Section 112 as stated by applicant. Thus, the rejection is maintained.**

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Claims 1-7,9-16,19-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is meant by "raw enzyme and raw enzyme weight." Although, applicant defines "raw enzyme and raw enzyme weight" it is suggested that "crude enzyme" may better describe applicant's invention. Further, applicant fails to present "enzyme weight" in a standard form of activity as is known in the art and as recommended by Methods of Enzymology. A clarification with respect to applicant's enzyme method is advised.

Claim 24 and 34 recites the limitation "undiluted enzyme solution". There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The previous/prior rejection of claims 1-3,6,7,10,19,20 rejected under 35 U.S.C. 102(b) as being anticipated by Bailey et al (US 4,204,041,1980) has been **withdrawn**.



The previous/prior rejection of claims 1-6,9,19,20 rejected under 35 U.S.C. 102(b) as being anticipated by Lausten et al (US2002/0020668 A1) has been **withdrawn**.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6,9,10,19-23,27,28,29,31-33,37,39,40,42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lausten et al (US2002/0020668 A1).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution, preferably a hydrolase such as amylase, glucoamylase and cellulase, by treating with a purifying agent, activated carbon. The raw enzyme solution is diluted with water and removed by filtration. Such method may also be carried out through a column. The enzyme to carbon ratio is not to exceed 50:1, preferably 15:1. Additionally that if any cells are present in the solution, that they are filtered out.

Lausten teach the use of activated carbon in a fermentation broth, particularly with enzymes such as amylases and cellulases, to remove soluble impurities by purification improving the quality of a product (see abstract and 0015,0018-0046). The carbon is added at concentration of up to 2% w/w (see 0046). The enzyme solutions

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are further diluted with water before addition of carbon and further microfiltered (see examples 1 and 2), although they also teach the purification of such enzyme solutions with activated carbon may also be performed by such methods such as ultrafiltration, chromatographic methods, i.e. column method, adsorption and/or crystallization (see 0057). Lausten also teaches that the fermentation broth may be treated prior to the method by separating out solids by filtration, flocculation or centrifugation, i.e. removing cells if present (0043 and 0044).

Although the above references do not specifically state the enhancement of the enzyme activity, the method of treating a diluted enzyme solution with a purifying agent, activated carbon, is the same. Lausten does not teach the exact dilution amounts and ratios. However, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known

provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.”). See MPEP 2144.05

Claims 1-6,9,10,12,13,15-17,19-23,27,28,29,31-33,37,39,40,42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lausten et al (US2002/0020668 A1) in view of Shenoy et al (J. of Bioscience, vol 7, 1985) and [http://www.ap-lab.com/circular\\_dichroism.htm](http://www.ap-lab.com/circular_dichroism.htm).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution by treating with a purifying agent. The enzyme solution of enhanced activity is claimed to have a relative absorbance intensity lower than the raw enzyme solution, preferably in the CD spectral range of 205-230 nm. Applicant further claims the enzyme to be alpha-amylase.

As stated above, Lausten teach the use of activated carbon in a fermentation broth, particularly with enzymes such as amylases and cellulases, to remove soluble impurities by purification improving the quality of a product (see abstract and 0015,0018-0046). The carbon is added at concentration of up to 2% w/w (see 0046). The enzyme solutions are further diluted with water before addition of carbon and further microfiltered (see examples 1 and 2), although they also teach the purification of such enzyme solutions with activated carbon may also be performed by such methods such as ultrafiltration, chromatographic methods, i.e. column method, adsorption and/or crystallization (see 0057). Laustsen also teaches that the fermentation broth may be

treated prior to the method by separating out solids by filtration, flocculation or centrifugation, i.e. removing cells if present (0043 and 0044).

Laustsen does not teach a CD spectral ranges. Shenoy et al (J. of Bioscience, vol7, 1985) teach the purification of glucoamylases. They teach that the catalytic activity of a protein, i.e. enzyme is related to its "active" conformation, i.e. secondary and tertiary structure. The specific activity of the purified enzymes was three times higher than that of the original non-purified glucoamylase (see p.400). They teach that the UV (CD) spectra of glucoamylases from 3 species show peaks at 289-293, 279-282 and 257-259 nm (see p.400-402), but also reveal negative bands at 217-220, 208-210 (see p. 402).

Shenoy does not teach lower CD spectrum ranges such as those claimed by applicant nor alpha-amylase. Information found at [http://www.ap-lab.com/circular\\_dichroism.htm](http://www.ap-lab.com/circular_dichroism.htm) teaches that any change in structure of proteins will affect the CD spectral range, therefore a change in the spectral range appears to be an inherent property of purification, i.e, structural change, of a protein. Thus, one of ordinary skill in the art would be motivated and it would therefore be obvious to claim a CD spectral range lower than that of a raw enzyme solution given that a change in structure ultimately affects the CD spectrum. When purifying a protein such as enzymes, one would have a reasonable expectation of success in obtaining a CD spectrum range lower than that of the raw enzyme solution given that purification, enhancing the catalytic activity of an enzyme, ultimately alters the secondary and

tertiary structure, therefore altering the CD spectrum range. Further, it would be obvious to optimize these parameters through routine experimentation.

Also it would be obvious to use other hydrolase enzyme such as alpha-amylase because Lausten teach the use of activated carbon in a fermentation broth, particularly with enzymes such as amylases and cellulases, to remove soluble impurities by purification improving the quality of a product (see abstract and 0015,0018-0046). Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to purify an enzyme such as alpha-amylase with activated carbon as taught by Lausten and would have a reasonable expectation of success in obtaining a CD spectral range lower than that of the raw enzyme solution given what is known in the art of the change in structure by purification of a protein.

Claims 1-6,9,10,11,14,19-23,27,28,29,31-33,37,39,40,42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aikat et al (Biotechnology Letters, vol 23, 2001,p.295-301) in view of Lausten et al (US2002/0020668 A1).

Applicant claims a method of enhancing the intrinsic activity of an enzyme solution, specifically a hydrolase, by treating with a purifying agent, activated carbon, and further removing the activated carbon from the enzyme solution by centrifugation. The purified enzyme solution is said to have a CD and UV distinct from that of the raw enzyme solution, specifically 30 nm less and the enzyme to carbon ratio is not to exceed 15:1.

Aikat et al teach the purification of protease by activated charcoal, i.e. activated carbon. They demonstrate the purification by activated charcoal in terms of fold purification and by electrophoretic analysis (see introduction). The enzyme solution was mixed with activated charcoal and allowed to react for a specific period of time prior to centrifugation, thus removing the activated carbon, at which time the supernatant was examined by spectroscopy. Further analysis was carried out by electrophoresis (see p. 296). The enzyme solution (1 ml) was treated with 50 to 150 mg of activated charcoal, although 75 mg of charcoal was selected as their optimum ratio. By gel analysis they observed the removal of almost all of the smaller proteins, confirming the purifying action of activated charcoal.

Further, Aikat diluted the crude enzyme solution 10 times to bring its absorbance within the range of that of charcoal-treated enzyme, which shows distinct troughs at 260 nm and a peak at 280nm. In the crude diluted solution there appeared to be a peak at 260 nm and no valley (see p.299 to 300).

Aikat does not teach diluting the raw enzyme solution prior to treating with a purifying agent. However, as stated above Lausten teach diluting an enzyme solution prior to treating the activated carbon. Thus, at the time of the invention it would have been obvious to one of ordinary skill in the art to dilute an enzyme solution prior to treatment because the prior art teaches dilution prior to treatment with activated carbon. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to have diluted an enzyme solution prior to purification with activated

carbon with a reasonable expectation for successfully enhancing the intrinsic activity of such solution because the art teaches such success when using the claimed enzyme solution and purifying agent.

### ***Response to Arguments***

Applicant's arguments with respect to claims 1-3,6,7,10,19,20 over Bailey have been considered but are moot in view of the new ground(s) of rejection.

Applicants 132 Declaration filed 5/2/2007 fails to show evidence commensurate in scope with the present application. Specifically, applicant has done a comparison, in Fig.1 and 2, of a native enzyme solution, the enzyme solution processed through activated carbon, and that of amylase produced by the method claimed, i.e. dilution and processing through an activated carbon column. It is unclear how one could conclude that such a graph and comparison would provide unexpected results commensurate in scope with applicant's invention. Applicant also does not provide how such activity is being measured, i.e. specific activity measured in the units as known in Enzymology. Applicant should do a side-by-side comparison of the diluted enzyme **without** being processed with activated carbon. There is something to be said of an enzyme solution which has been diluted and its endogenous inhibitors affecting an increase after dilution, i.e. an inhibitor which possesses a low affinity for the enzyme. Changes in activity or inhibition with dilution are a function of the specific enzyme and amount of enzyme in the initial enzyme solution. Further, activated carbon is a known absorbent, therefore the effect may be explained by the fact that the small molecules present in

solution are inhibitors of the enzymes therefore binding to the activated carbon, allowing a more pure enzyme to remain. The offices position is that a more effective comparison may include additionally the same diluted enzyme solution not processed with activated carbon compared to the same volume, amount of enzyme diluted solution which has been processed with activated carbon. It is unclear from the Figure legends in applicants declaration which boxes correspond to the white and grey shaded bars.

Applicant arguments in response to the Lausten reference have been considered, however, applicant argues that Lausten discloses an enzyme dilution of 1:1, while this is true, they also disclose at least a two part dilution, see example 2, which teaches at least 2 parts. Applicant also does not show in the submitted Declaration that a dilution of 2:1 is better than or has an unexpected increase of activity compared to a 1:1 dilution. Applicant also argues that Lausten dilutes an enzyme broth which contains cells and in contrast applicants invention contains a broth in which the cells have been filtered out first. Applicant does not specifically claim whether or not the cells are present and/or if they have been filtered out. Thus, applicants arguments are not commensurate in scope with the claimed invention. Applicant argues that the Declaration submitted on 5/2/2007 teaches that filtering an enzyme solution through an activated carbon column does not inherently increase enzyme activity. However, as stated above, the showing in the declaration does not accurately show or compare "dilution, removal of cells if present, and then contacting with the activated carbon" which results in a surprising enhancement of activity (see p.11 of Arguments). Applicant



merely compares the native enzyme solution, the solution with activated carbon and that which has been diluted. Therefore, the arguments are not persuasive.

It is noted that applicant has submitted many documents teaching away from applicants claimed invention, i.e. attempting to overcome the Offices inherency rejection and to show unexpected results.

Regarding applicant's arguments directed towards the Shenoy reference, i.e. that Shenoy does not teaches purification resulting in activity three times higher than the original non-purified glucoamylase, rather compared to a parent strain. While this has been considered, applicant does not specifically claim nor show in the Declaration, purification of an original non-purified enzyme. Applicant actually compares in the declaration dated 5/2/2007, an already purified commercial enzyme to a diluted enzyme purified by the claimed method. Thus, applicant's arguments are not commensurate in scope with the present invention.

Applicant's arguments directed to spectral change continue to be confusing. Applicant is arguing that it is the goal of purification to avoid a structural and spectral change, yet claim a spectral change, which is distinct from the "raw enzyme solution", as in claim 11,12,13,30. The argument is contradictory. The examiner is well aware of the fact that CD is used after the fact to determine alteration in the structure. Applicant argues that their method is unique in that it leads to a change in protein structure, due to catalytic modification of the protein. Shenoy also teach that the catalytic activity of a protein, i.e. enzyme is related to its "active" conformation, i.e. secondary and tertiary structure. They state that the ideal purification would preserve protein structure and

avoid change in spectral properties, yet claim that their method is unique in that it leads to a change in protein structure, due to catalytic modification of the protein. This argument is not understood.

Applicant argues that the art does not teach or suggest the claimed process of contacting a diluted enzyme solution to activated carbon, in which the cells have been removed. Laustsen by themselves do teach such a process.

In response to applicant previous argument dated 10/19/2006 p.11 of the response, applicant had argued that they do not claim a specific CD spectra, but rather that there had been a change in structure as supported by CD spectra. The examiner's argument, "Applicant absolutely claims a specific CD spectra in claims 12-15, thus applicants arguments are not supported by the claims." Applicant now argues in the response filed 5/2/2207 that this statement is not understood and that claims 11-15 show changes in the defined spectra in the claims. Therefore, in claims 12, applicant **does claim** a specific CD spectral range.

Applicant argues that one of skill in the art would not have been motivated to dilute an enzyme prior to purification with activated carbon because the art does not suggest so. However, Laustsen does teach dilution prior to purification. In response to applicant's arguments that there is no motivation or teaching/suggestion, applicant is advised that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*,--USPQ2d--,slip op at 20,(Bd. Pat. App & Interf. June 25, 2007)

(citing *KSR*, 82 USPQ2d at 1396) (available at

<http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>)

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tiffany Gough

/Ruth A Davis/

Primary Examiner, AU 1651